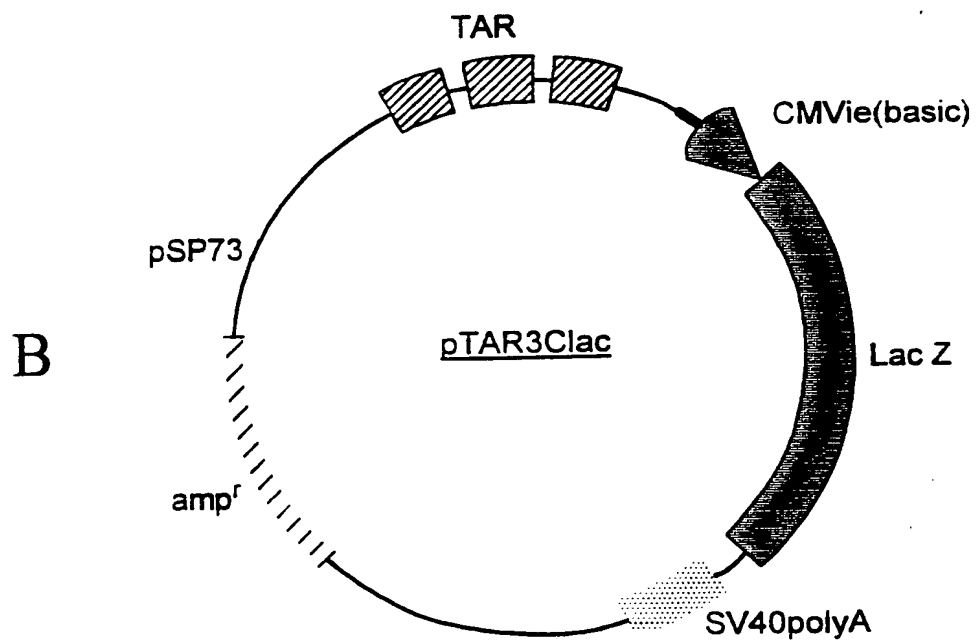
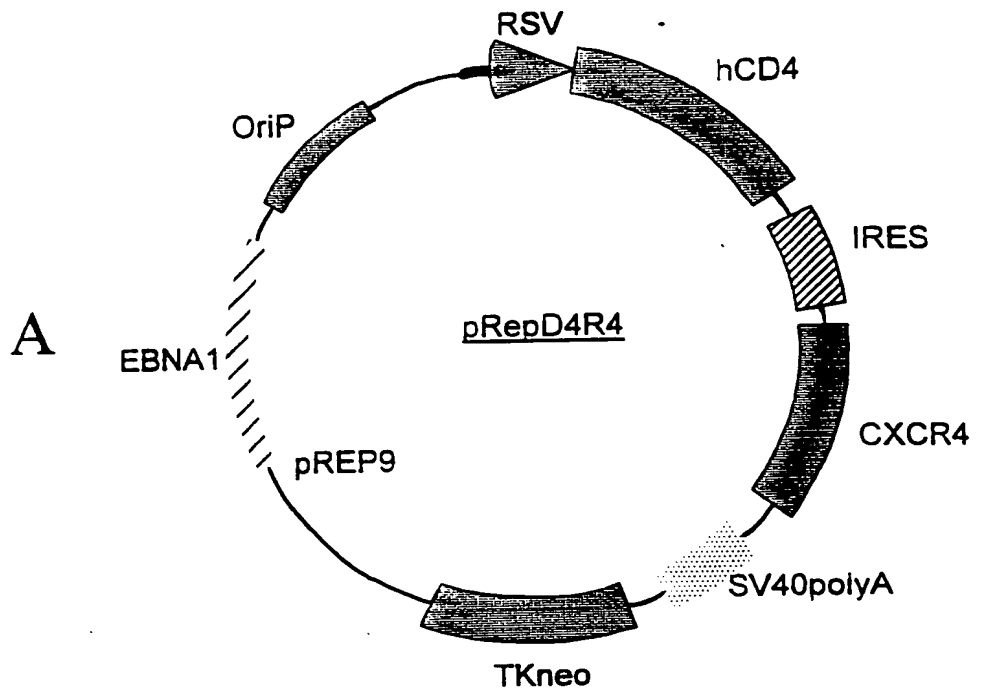


**FIG. 1**



**FIG. 2**

FIG. 3

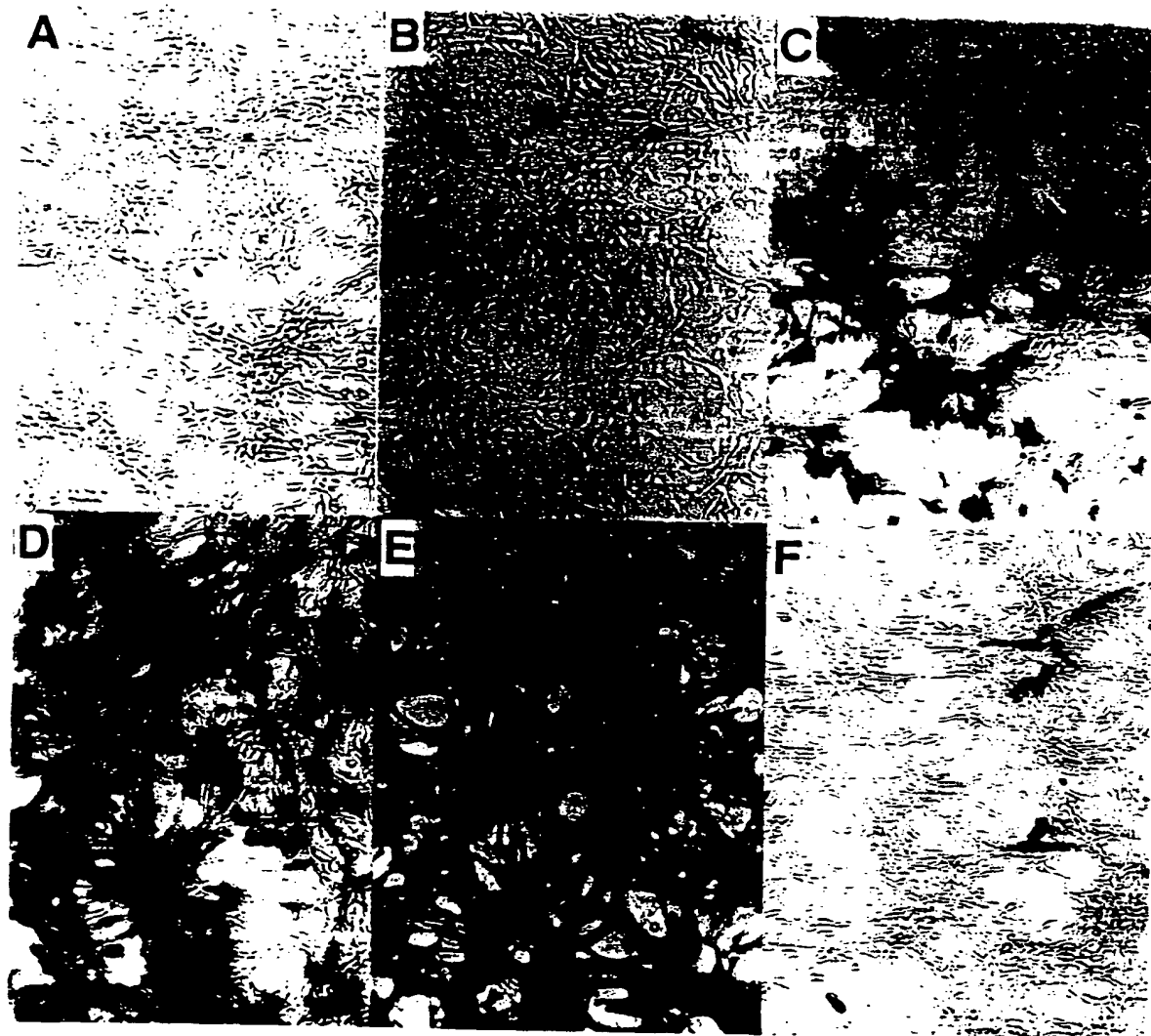


FIG. 4A

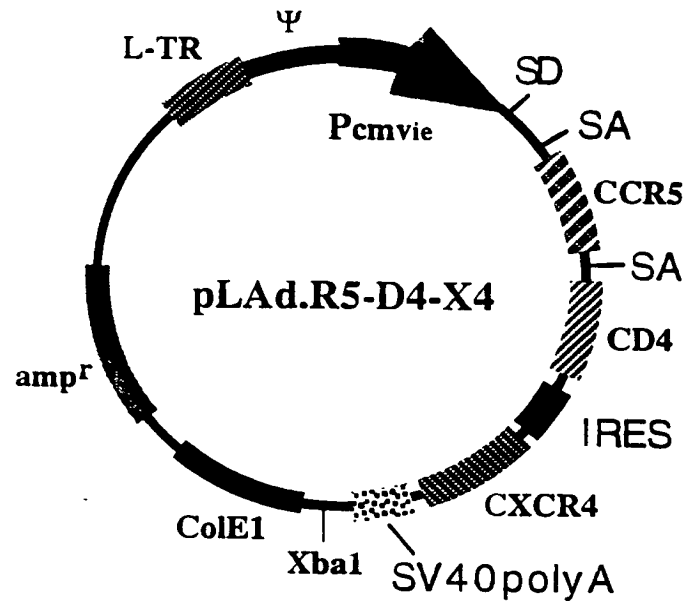


FIG. 4B

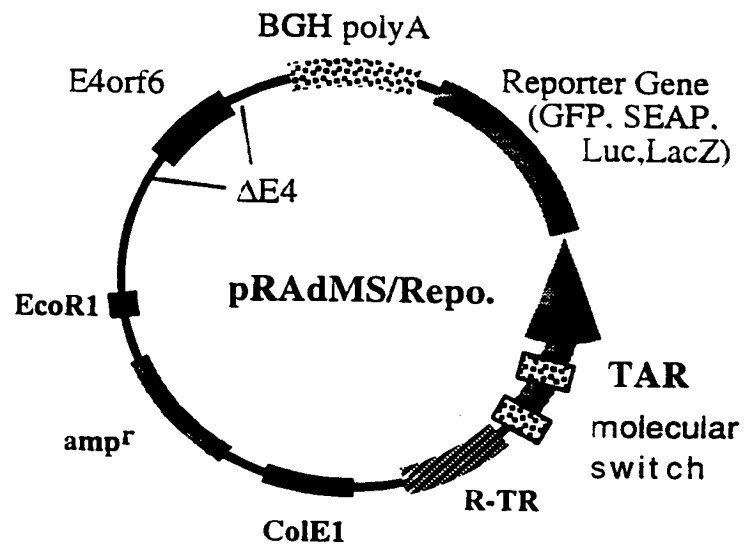


FIG. 5A

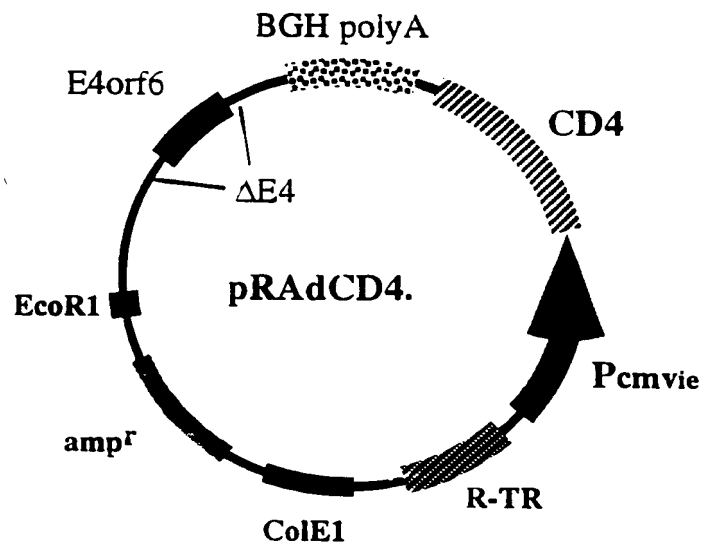
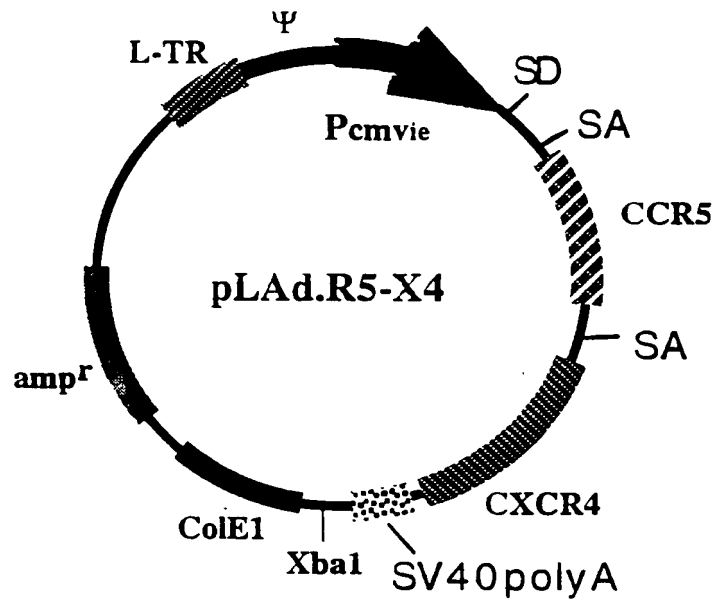


FIG. 5B

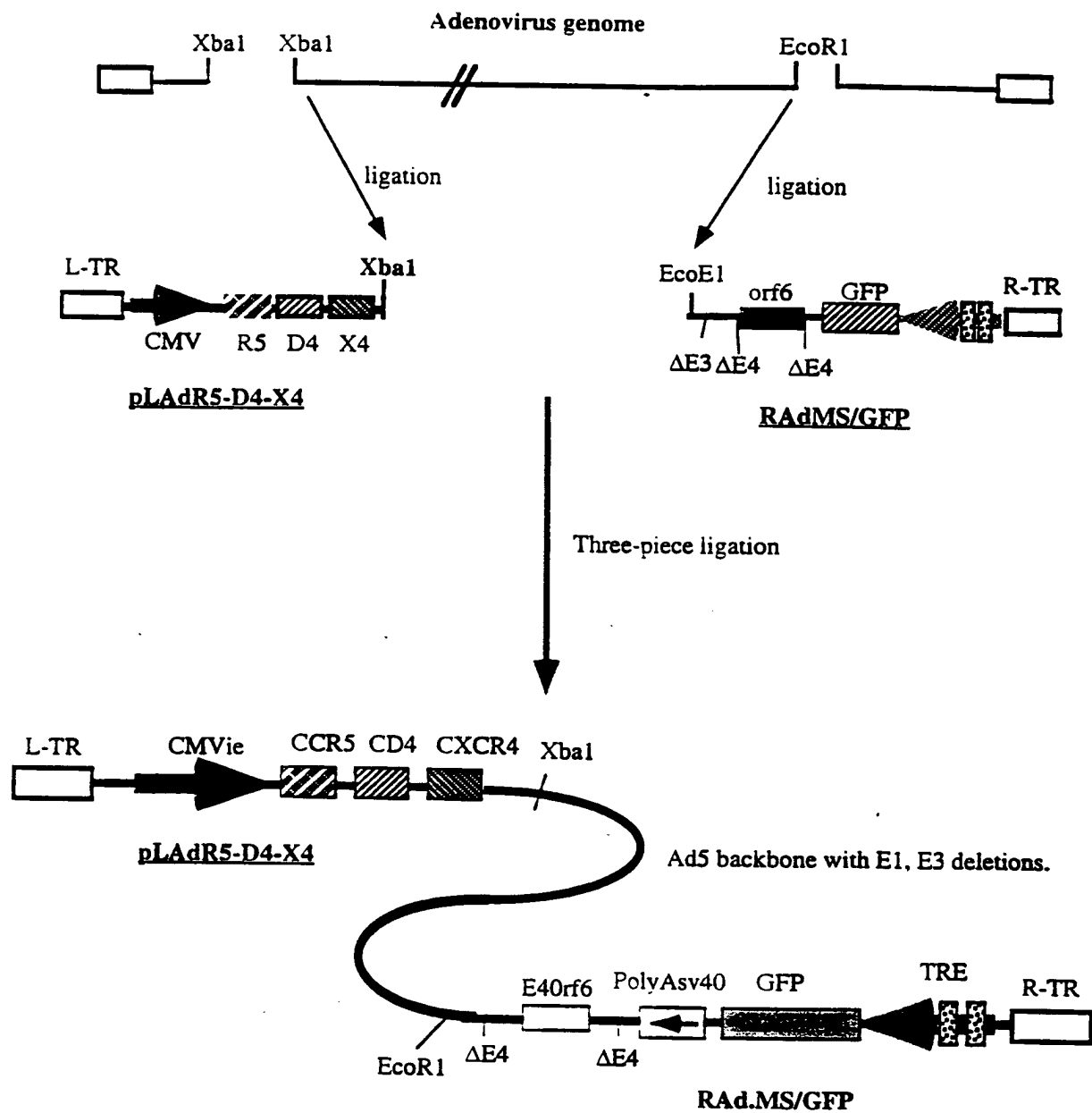


FIG. 6

# pLAd-CCR5.CXCR4 (9 Kb)

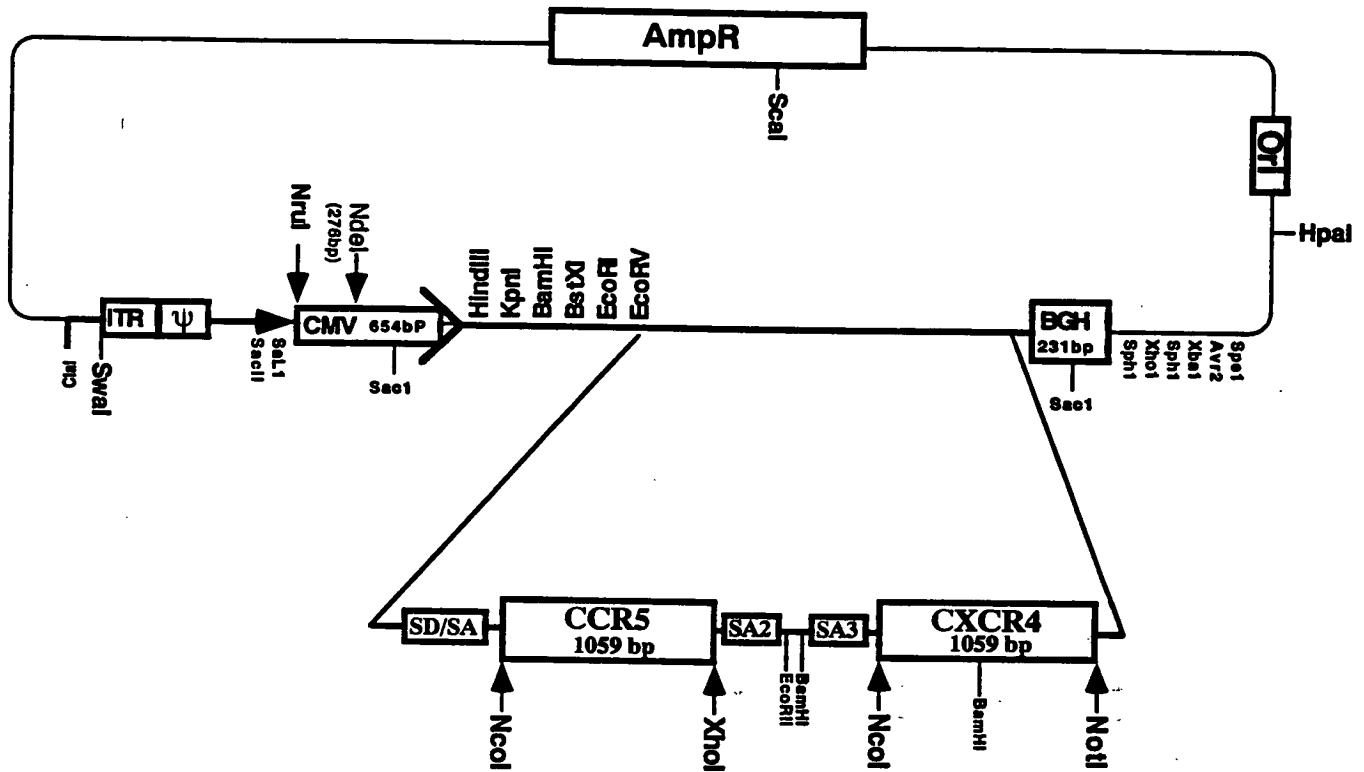


FIGURE 7A

# pRAd.CMV.Fiber.ORF6-CD4.CXCR4 (~14.8 Kb)

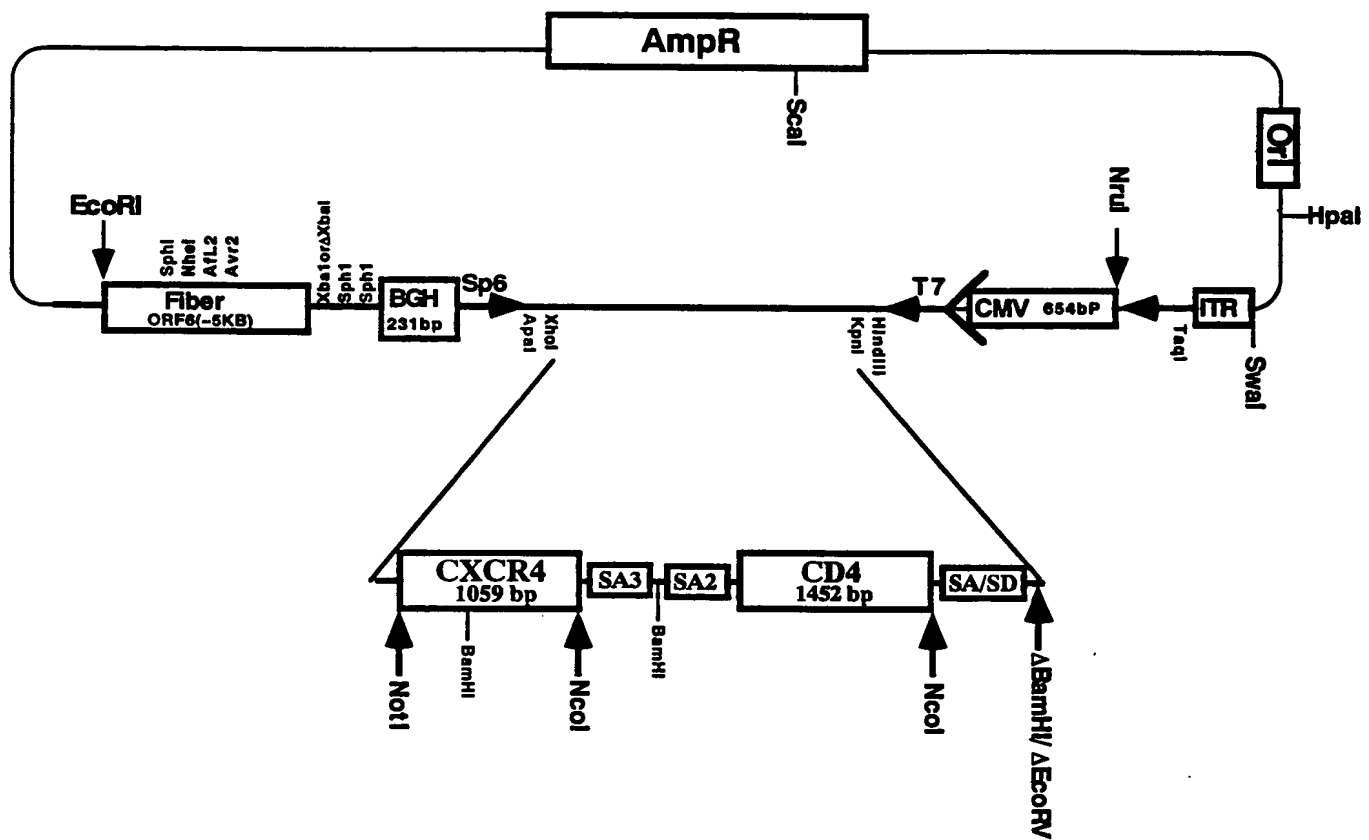
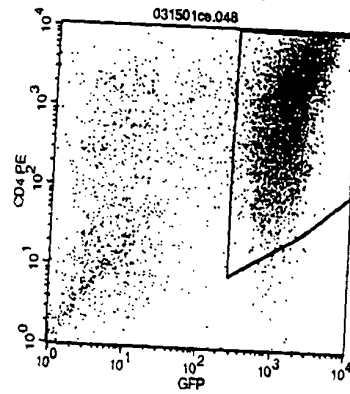


FIGURE 7B



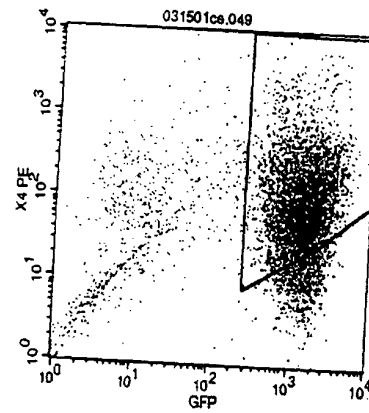
**FIGURE 8**

**A.**



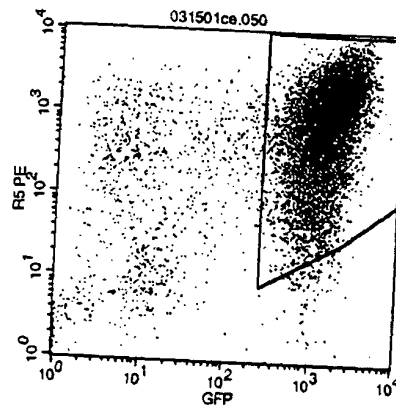
CD4 Expression Level: 84.0 %

**B.**



CXCR4 Expression Level: 77.7 %

**C.**



CCR5 Expression Level: 89.6 %

FIGURE 8 D



E



F



**FIGURE 8G**

#	Cell Types	Infected	Fluorescent-PE Ab	All %Gated	M1 %Gated	All Mean	M1 Mean	All Geo Mean	M1 Geo Mean
1	HUT78	non	mouse IgG 2ak-PE	100	1.2	4.04	21.74	3.35	18.83
2		non	CD4-PE	100	99.92	628.77	629.25	484.56	486.22
3		non	CXCR4-PE	100	65.29	24.21	32.1	18.27	26.74
4		non	CCR5-PE	100	1.56	4.14	27.48	3.34	23.44
5	CEM-NKr-R5	non	mouse IgG 2ak-PE	100	3.12	3.74	19.8	3.05	16.24
6		non	CD4-PE	100	99.6	343.3	344.67	285.47	290.65
7		non	CXCR4-PE	100	98.99	65.93	66.55	53.8	55.13
8		non	CCR5-PE	100	66.66	38.76	55.64	16.91	32.66
9	Molt-4-R5	non	mouse IgG 2ak-PE	100	1.15	3.87	31.78	3.31	20.82
10		non	CD4-PE	100	57.1	35.1	57.41	15.58	39.05
11		non	CXCR4-PE	100	91.44	73.1	79.25	47.6	57.08
12		non	CCR5-PE	100	59.66	37.1	57.94	17.75	38.66
13	CEM-A	non	mouse IgG 2ak-PE	100	0.59	3.38	14.07	3.01	12.31
14		non	CD4-PE	100	94.44	98.93	104.5	62.23	73.75
15		non	CXCR4-PE	100	99.69	87.06	87.31	69.86	70.36
16		non	CCR5-PE	100	0.24	3.06	33.62	2.7	17.45
17	MEGI	non	mouse IgG 2ak-PE	100	2.1	6.17	19.43	5.45	18.61
18			CD4-PE	100	96.7	126.69	130.76	97.19	106.47
19			CXCR4-PE	100	50.34	16.25	22.6	14.18	21.27
20			CCR5-PE	100	2.03	6.34	20.31	5.62	19.43
21	Indicator#44	3R122900	mouse IgG 2ak-PE	100	1.86	4.96	27.72	4.16	19.95
22		MOI, 30	CD4-PE	100	95.19	577.67	584.4	271.07	324.48
23			CXCR4-PE	100	95.78	177.72	185.15	108.28	121.08
24			CCR5-PE	100	92.42	258.22	278.69	132.99	167.66
25	Indicator#44	3R122900	mouse IgG 2ak-PE	100	2.08	5.11	32.83	4.21	23.34
26		MOI, 60	CD4-PE	100	93.42	894.83	957.23	393.37	518.33
27			CXCR4-PE	100	93.68	219.61	233.8	125.85	150.97
28			CCR5-PE	100	91.64	369.08	401.96	175.48	232.68

**FIGURE 8G - Cont.**

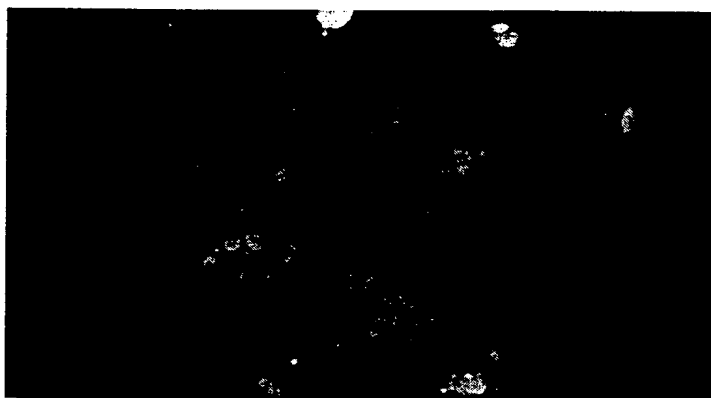
#	Cell Types	Infected	Fluorescent-PE Ab	All %Gated	M1 %Gated	All Mean	M1 Mean	All Geo Mean	M1 Ge Mean
29	Hela	non	mouse IgG 2ak-PE	100	1.09	3.85	34.76	3.06	23.76
30		non	CD4-PE	100	1.28	5.05	28.9	4.22	19.37
31		non	CXCR4-PE	100	94.37	69.86	73.42	53.53	59.26
32		non	CCR5-PE	100	2.1	5.29	21.55	4.45	18.95
33	PBMC	non	mouse IgG 2ak-PE	100	0.13	4.02	237.03	2.89	164
34		non	CD4-PE	100	42.6	315.27	731.4	37.45	655.64
35		non	CXCR4-PE	100	20.35	35.15	101.11	18.07	89.8
36		non	CCR5-PE	100	0.24	4.88	316.55	3.03	180.47

**FIGURE 9**

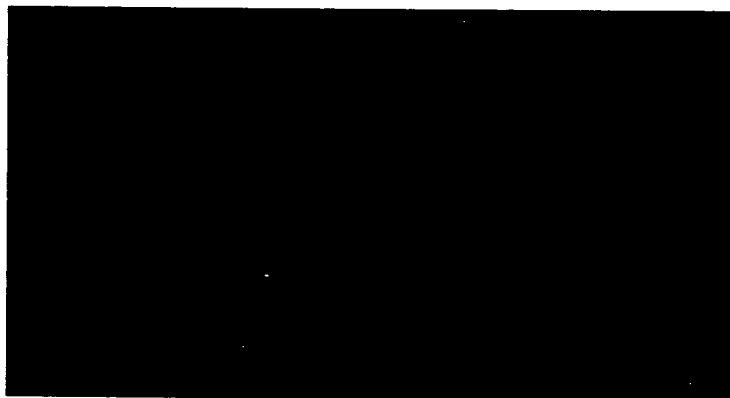
**A.**



**B.**



**C.**



**FIGURE 10**

**Table 1.** Viral infection of Indicator Cells by HIV-1 Subtypes

<b>Cat. No.</b>	<b>Inhibition by IIIB Ab (4 µl)</b>	<b>Subtype (gag/env)</b>	<b>Viral Titer (ip/ml)</b>	<b>Co-receptor</b>	<b>NIH p24 (ng/ml)</b>	<b>Phenotype</b>
398	(HTLV-IIIB/H9) 100% (50 ip) 88% (225 ip) 83% (400 ip)	B/B	2.0 x 10 <sup>5</sup>	X4	-	SI (+++)
1650	(92UG029) 16% (170 ip) 35% (600 ip)	A/A	8.9 x 10 <sup>3</sup>	X4	47	SI (+)
1996	(93RW002)	/A	1.9 x 10 <sup>2</sup>	R5	121	SI
2304	(94UG103) 29% (37 ip) 12% (185 ip)	/A	3.7 x 10 <sup>3</sup>	R5,X4	155	SI (++)
1658	(92TH014)	B/B	1.2 x 10 <sup>4</sup>	R5	177	SI
2308	(93BR012) 16% (120ip) 38% (660 ip)	/B	1.2 x 10 <sup>4</sup>	R5	316	SI (+)
1777	(92BR025) 8% (120 ip) 10% (500 ip)	C/C	1.0 x 10 <sup>4</sup>	R5	164	NSI*(±)
4164	(98CN006)	C/C	8.8 x 10 <sup>3</sup>	R5	160	SI
1684	(92UG005) 23% (400 ip) 22 % (1200 ip)	D/D	1.7 x 10 <sup>4</sup>	R5	225	SI (+)
1952	(93UG065)	D/D	1.6 x 10 <sup>3</sup>	X4	245	SI
2166	(93TH053)	/E	1.4 x 10 <sup>3</sup>	X4	45	NSI*
2167	(93TH054)	/E	2.4 x 10 <sup>3</sup>	R5	58	SI
2314	(93BR019) 40% (86 ip) 23% (430 ip)	/BF	8.6 x 10 <sup>3</sup>	X4	128	SI (++)
2329	(93BR020)	F/F	5.7 x 10 <sup>3</sup>	R5, X4	169	SI
2338	(93BR029) 33% (300 ip)	B/F	5.8 x 10 <sup>3</sup>	R5	185	SI (+++)
4143	(BCF13) 32% (180 ip)	Group O	2.9 x 10 <sup>4</sup>	-	-	SI (+++)

All viruses were titrated between day 3 and day 4 postinfection

\* At day 4, there were no syncytial formed.

**FIGURE 11**

Comparison GenPhar Indicator with MAGI Cells								
HIV	HIV Strains	Sources	Catalogue	Co-Receptor	Indicator#44 (lp/ml)	MEGI (lp/ml)	Indicator/MEGI	
Wild type	IIIB	NIH	398	X4	75,000	66,000	1.14	
Patient's Isolates	JM	GenPhar, INC		X4	1,050	490	2.14	
Patient's Isolates	92UG001	NIH	1647	X4, R5	5,200	1,900	2.74	
Patient's Isolates	93TH054	NIH	2167	R5	4,800	0	0.00	
Patient's Isolates	93BR020	NIH	2329	X4R5	5,250	530	9.91	

FIGURE 12

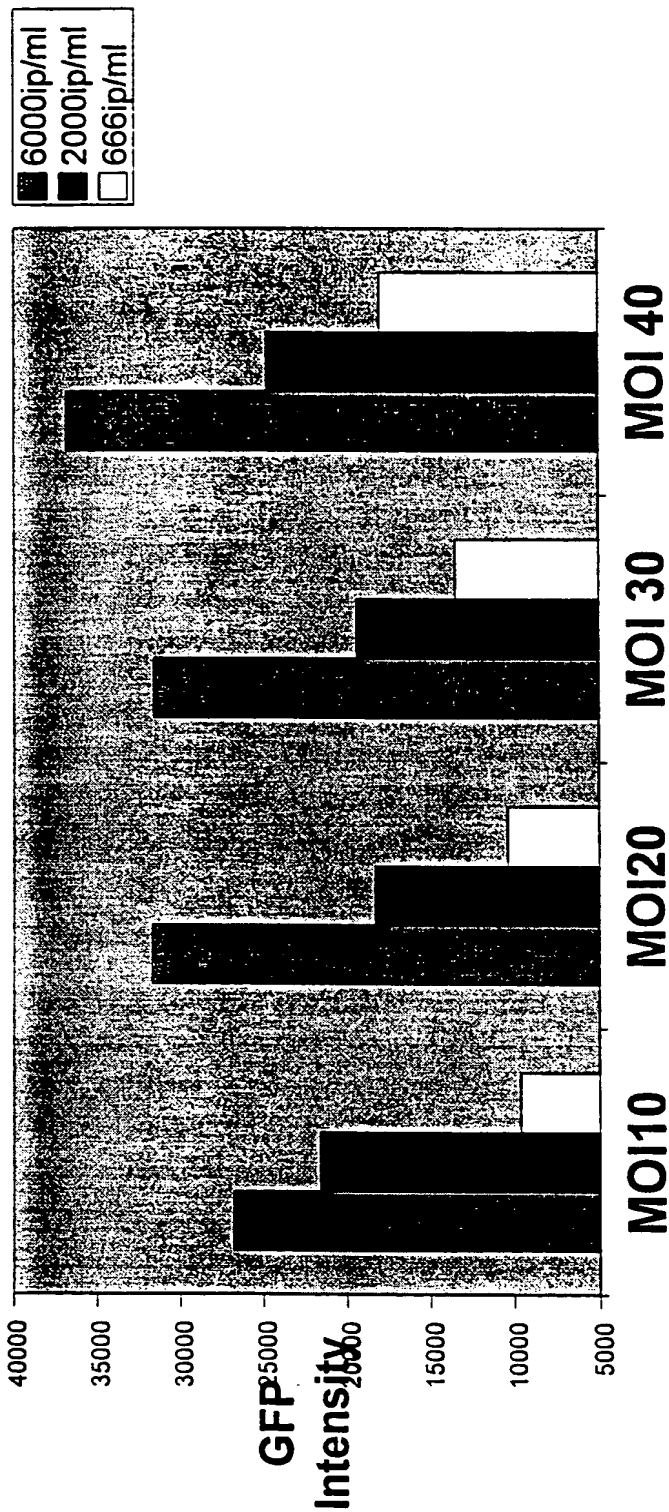
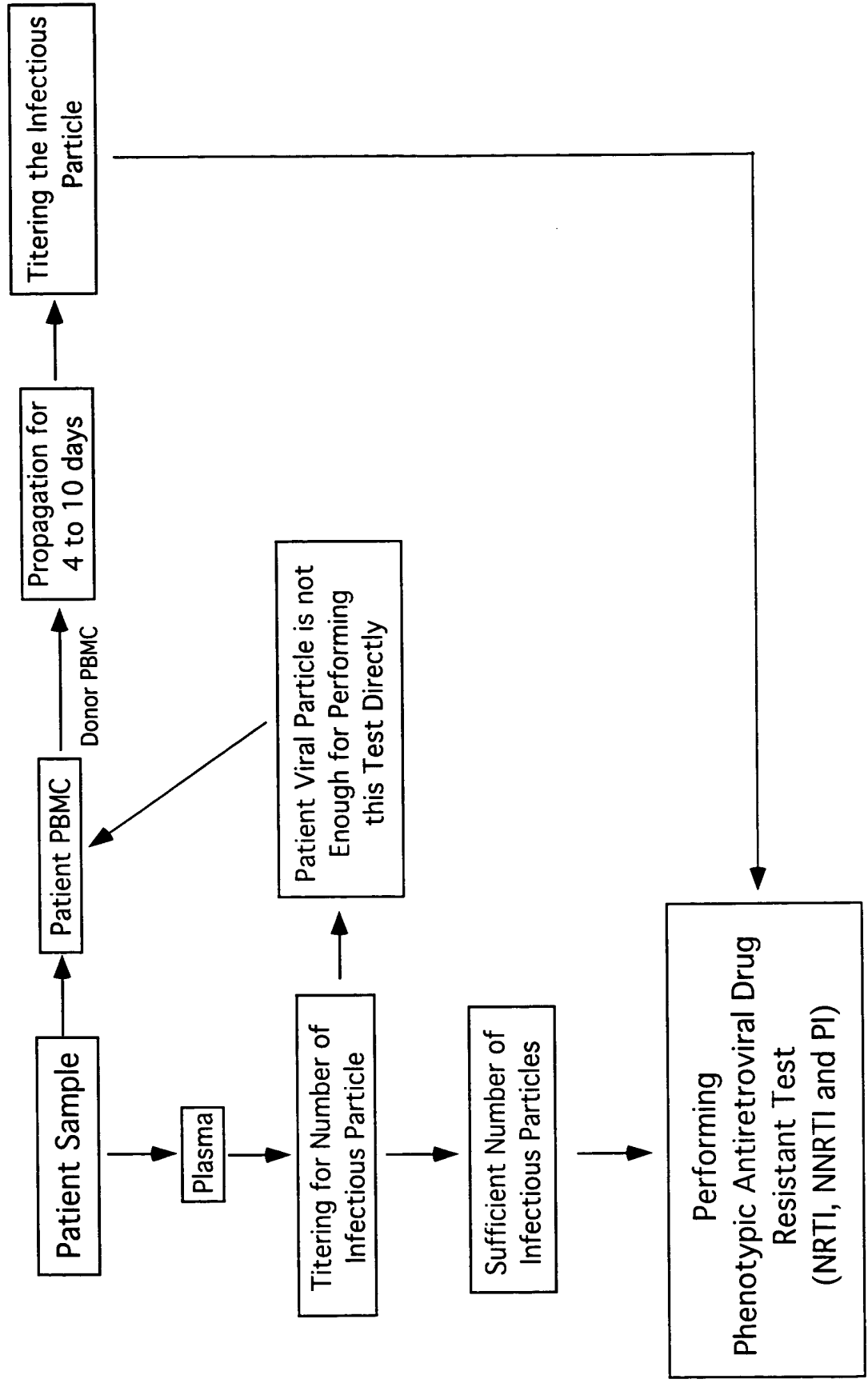


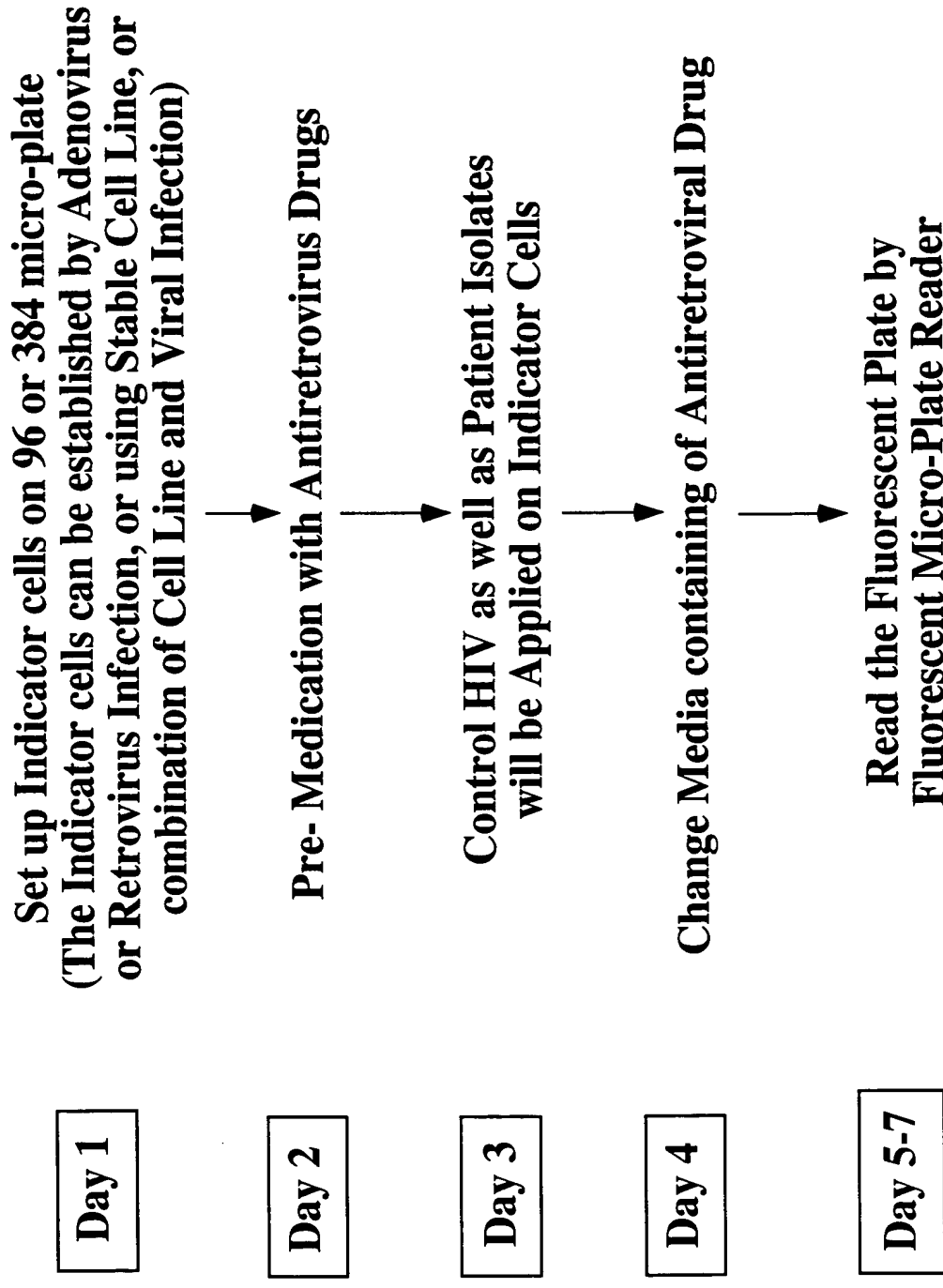


FIGURE 13



**FIGURE 14**

## **Phenotypic Antiretroviral Drug Resistant Test for NRTI and NNRTI**



## **FIGURE 15**

### **HIV DRUG RESISTANCE ASSAY FOR PI**

#### **PRIMARY PLATE**

**Set Up Infection Plate of Cells Containing 3 HIV Receptors with a Sample containing HIV in the Presence of the PI Drug to be tested for a Suitable Period of Time**

#### **SECONDARY PLATE**

**- Day 1      Set Up Indicator Cells Containing 3 HIV Receptors as well as a Reporter Gene for Monitoring HIV Infection**



**Day 1      Transfer the Supernatant of the Culture in the Primary Plate to the Indicator Cells for Titration of HIV**



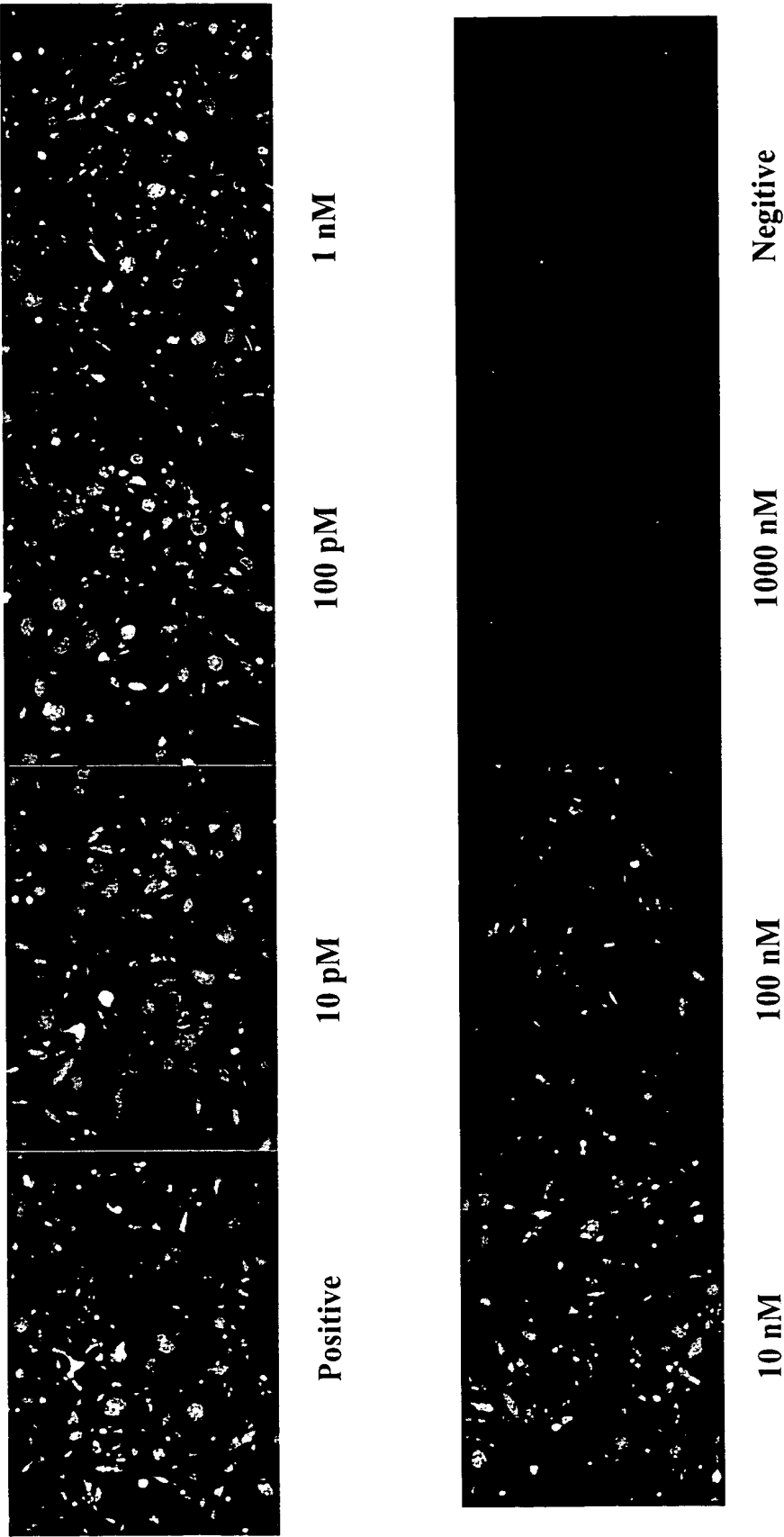
**Day 2      Change Media**



**Day 3-4      Read Plates by Fluorescent Micro-Plate Reader**

FIGURE 16

Phenotypic Antiretroviral Drug Resistant Test



**FIGURE 17A**

	Drug Name		Brand Name	Virologic Mean IC <sub>50</sub> (CND0)	NIH IC <sub>50</sub> (Other Virus)	NIH IC <sub>50</sub> (III-B) (Other Cells)	GenPhar Reference: IC <sub>50</sub> Values		Patient		
	Drug	CS	G								
uM	NRTI	Zidovudine	Retrovir	0.03	0.05	0.05	0.0008	IC <sub>50</sub> Shift	0.026	ZDV	
		Didanosine	Videx	4.57	0.46	8	3.03	IC <sub>50</sub> Shift	32.5	ddl	
		Stavudine	Zerit	0.66	0.009	0.05	0.077	IC <sub>50</sub> Shift	26.3	d4T	
		Zalcitabine	Hivid	0.68	0.011	0.3	0.115	IC <sub>50</sub> Shift	8.679868	ddC	
		Lamivudine	Epivir	1.77	>100		0.404	IC <sub>50</sub> Shift	5.5	3TC	
		Abacavir	Ziagen	1.74		4	0.827	IC <sub>50</sub> Shift	71.43	ABC	
	NtRTI	Tenofovir	Viread		0.04	8.5	10.3	IC <sub>50</sub> Shift	201.5	TNV	
		Nevirapine	Viramune	78		48	45.95	IC <sub>50</sub> Shift	498.8	NVP	
	nM	NNRTI	Delavirdine	Rescriptor	32	0.0001	0.1		IC <sub>50</sub> Shift	14,300	DLV
			Efavirenz	Sustiva	2	0.003	1.575	1.01	IC <sub>50</sub> Shift	311.2	EFV

FIGURE 17B

	Drug Name      Brand Name		Virologic Mean IC <sub>50</sub> (CNDQ)	NIH IC <sub>50</sub> (Other Virus) PBMC	NIH IC <sub>50</sub> (III-B) (Other Cells)	GenPhar Reference: IC <sub>50</sub> Values		Patient	
								JL	Drug
		G							
uM	NRTI	Zidovudine	Retrovir	0.03	0.05	0.0008	IC <sub>50</sub> Shift	0.074	ZDV
		Didanosine	Videx	4.57	0.46	3.03	IC <sub>50</sub> Shift	92.5	
		Stavudine	Zerit	0.66	0.009	0.077	IC <sub>50</sub> Shift	57.8	ddl
		Zalcitabine	Hivid	0.68	0.011	0.115	IC <sub>50</sub> Shift	2.3	d4T
		Lamivudine	Eplivir	1.77	>100	0.404	IC <sub>50</sub> Shift	29.87	
		Abacavir	Ziagen	1.74		0.827	IC <sub>50</sub> Shift	0.4	ddC
	NRTI	Tenofovir	Viread		0.04	10.3	IC <sub>50</sub> Shift	3.48	
		Nevirapine	Viramune	78		45.95	IC <sub>50</sub> Shift	6.2	3TC
	NNRTI	Delavirdine	Rescriptor	32	0.0001		IC <sub>50</sub> Shift	10.3	ABC
		Efavirenz	Sustiva	2	0.003	1.01	IC <sub>50</sub> Shift	12.45	
							IC <sub>50</sub> Shift	23.5	TNVP
nM	NNRTI						IC <sub>50</sub> Shift	2.28	
							IC <sub>50</sub> Shift	98,700	NVP
							IC <sub>50</sub> Shift	2148	DLV
							IC <sub>50</sub> Shift		EFV
							IC <sub>50</sub> Shift	127.1	
							IC <sub>50</sub> Shift	125.8	

FIGURE 17C

	Drug Name      Brand Name		Virologic Mean IC <sub>50</sub> (GNDO)	NIH IC <sub>50</sub> (Other Virus)	NIH IC <sub>50</sub> (III-B) (Other Cells)	GenPhar Reference: IC <sub>50</sub> Values		Patient	
								JM	Drug
								G	
uM	NRTI	Zidovudine	Retrovir	0.03	0.05	0.0008	IC <sub>50</sub> Shift	0.042 52.5	ZDV
		Didanosine	Videx	4.57	8	3.03	IC <sub>50</sub> Shift	8.3 2.74	ddl
		Stavudine	Zerit	0.66	0.05	0.077	IC <sub>50</sub> Shift	4.6 59.74	d4T
		Zalcitabine	Hivid	0.68	0.3	0.115	IC <sub>50</sub> Shift	0.036 0.31	ddC
		Lamivudine	EpiVir	1.77	>100	0.404	IC <sub>50</sub> Shift	0.26 0.64	3TC
		Abacavir	Ziagen	1.74	4	0.827	IC <sub>50</sub> Shift	2.4 2.9	ABC
		Tenofovir	Viread		8.5	10.3	IC <sub>50</sub> Shift	13.6 1.32	TNF
		Nevirapine	Viramune	78	48	45.95	IC <sub>50</sub> Shift	273 5.94	NVP
		Delavirdine	Rescriptor	32	0.1		IC <sub>50</sub> Shift		DLV
		Efavirenz	Sustiva	2	1.575	1.01	IC <sub>50</sub> Shift	37.4 37.03	EFV
nM	NNRTI								

Patient IC <sub>50</sub> , Shift, and R <sup>2</sup> Values for GenPhar Tru-Select (G) and Virlogic Phenosense (V) Assay Tests													
Drug Name	Brand Name	Virologic Mean IC <sub>50</sub> (CND0)	NIH IC <sub>50</sub> (Other Virus) PBMC	NIH IC <sub>50</sub> (III-B) (Other Cells)	GenPhar III-B IC <sub>50</sub> Values	CS		JL		JM		Drug	
						G	V	G	V	G	V	G	V
Saqinavir	Invirase	3		25	34.327	IC <sub>50</sub>	934		927		93.03		APV
						Shift	27.415757		27.21029		2.73071504		
						R <sup>2</sup>	0.86		0.78		0.90		
Ritonavir	Norvir	14	46	25	21.384	IC <sub>50</sub>	242.8		817.9		36.61		RTV
						Shift	6.775877		22.82533		1.02		
						R <sup>2</sup>	0.96		0.84		0.93		
Nelfinavir	Viracept	3	10	31	34.026	IC <sub>50</sub>	#DIV/0!		#DIV/0!		#DIV/0!		LPV
						Shift	584.7		945.6		16.41		
						R <sup>2</sup>	17.18		27.79		0.48		
Lopinavir	Aluviran	52				IC <sub>50</sub>	955.7		1151		384.5		NFV
						Shift	44.7		53.83		17.98		
						R <sup>2</sup>	0.83		0.85		0.92		
Amprenavir	Argenerase	12		7	34.068	IC <sub>50</sub>	124.6		824.7		33.56		SQV
						Shift	3.63		24.02		0.98		
						R <sup>2</sup>	0.92		0.83		0.95		

Patient IC <sub>50</sub> , Shift, and R <sup>2</sup> Values for GenPhar Tru-Select (G) and Virlogic Phenosense (V) Assay Tests														
Drug Name	Brand Name	Virologic Mean IC <sub>50</sub> (CND0)	NIH IC <sub>50</sub> (Other Virus) PBMC	NIH IC <sub>50</sub> (III-B) (Other Cells)	GenPhar III-B IC <sub>50</sub> Values	CS		JL		JM		Drug		
						G	V	G	V	G	V	G	V	
Saqinavir	Invirase	3		25	34.327	IC <sub>50</sub>	934		927		93.03		APV	
						Shift	27.415757		27.21029		2.73071504			
						R <sup>2</sup>	0.86		0.78		0.90			
Ritonavir	Norvir	14	46	25	21.384	IC <sub>50</sub>	242.8		817.9		36.61		RTV	
						Shift	6.775877		22.82533		1.02			
						R <sup>2</sup>	0.96		0.84		0.93			
Nelfinavir	Viracept	3	10	31	34.026	IC <sub>50</sub>	#DIV/0!		#DIV/0!		#DIV/0!		LPV	
						Shift	584.7		945.6		16.41			
						R <sup>2</sup>	17.18		27.79		0.48			
Lopinavir	Aluviran	52				IC <sub>50</sub>	955.7		1151		384.5		NFV	
						Shift	44.7		53.83		17.98			
						R <sup>2</sup>	0.83		0.85		0.92			
Amprenavir	Argenerase	12		7	34.068	IC <sub>50</sub>	124.6		824.7		33.56		SQV	
						Shift	3.63		24.02		0.98			
						R <sup>2</sup>	0.92		0.83		0.95			



FIGURE 18A

# Dose Response & IC<sub>50</sub> Shift Curves for ZDV

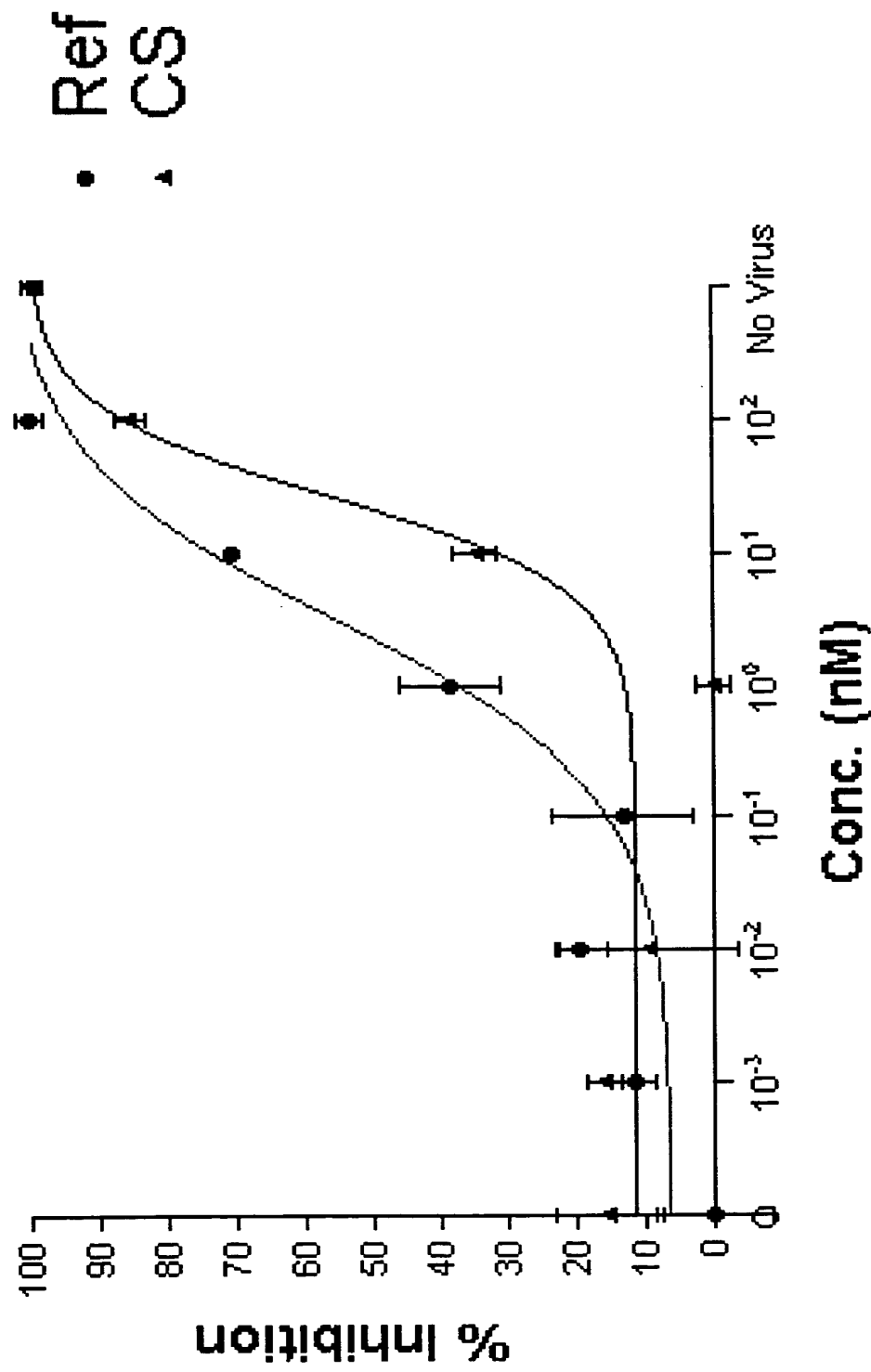


FIGURE 18B

## Dose Response & IC<sub>50</sub> Shift Curves for NVP

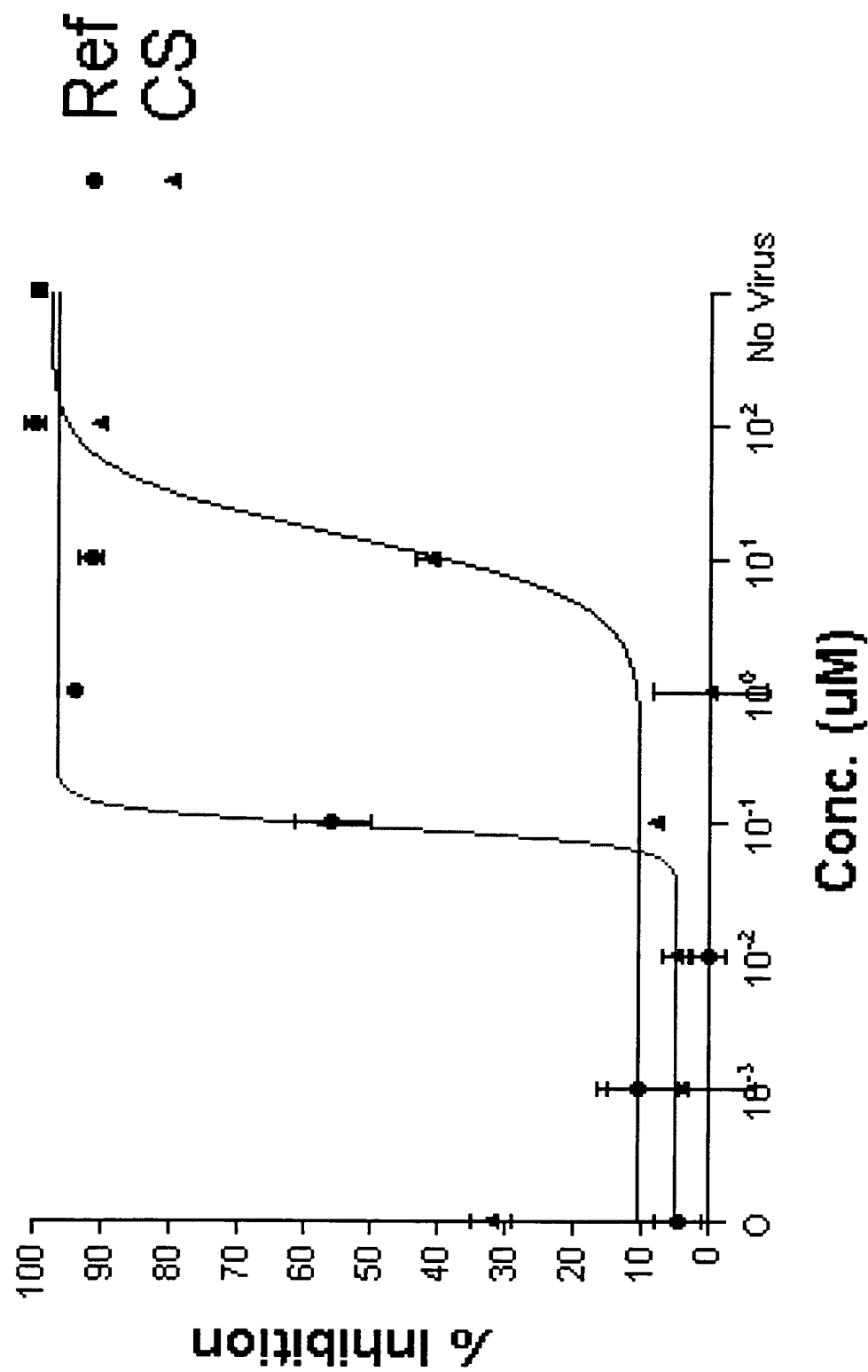


FIGURE 18C

## Dose Response & IC<sub>50</sub> Shift Curves for RTV

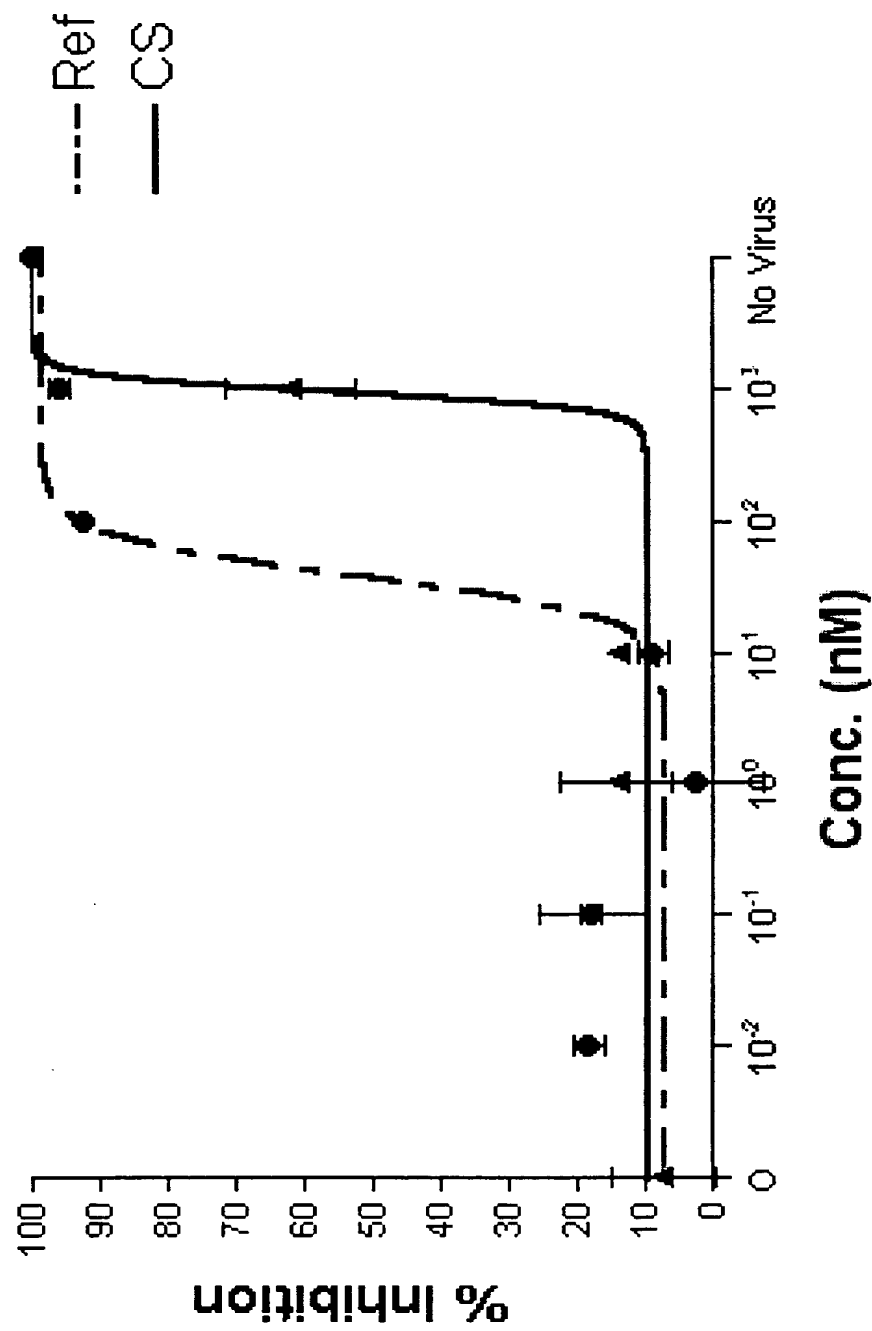
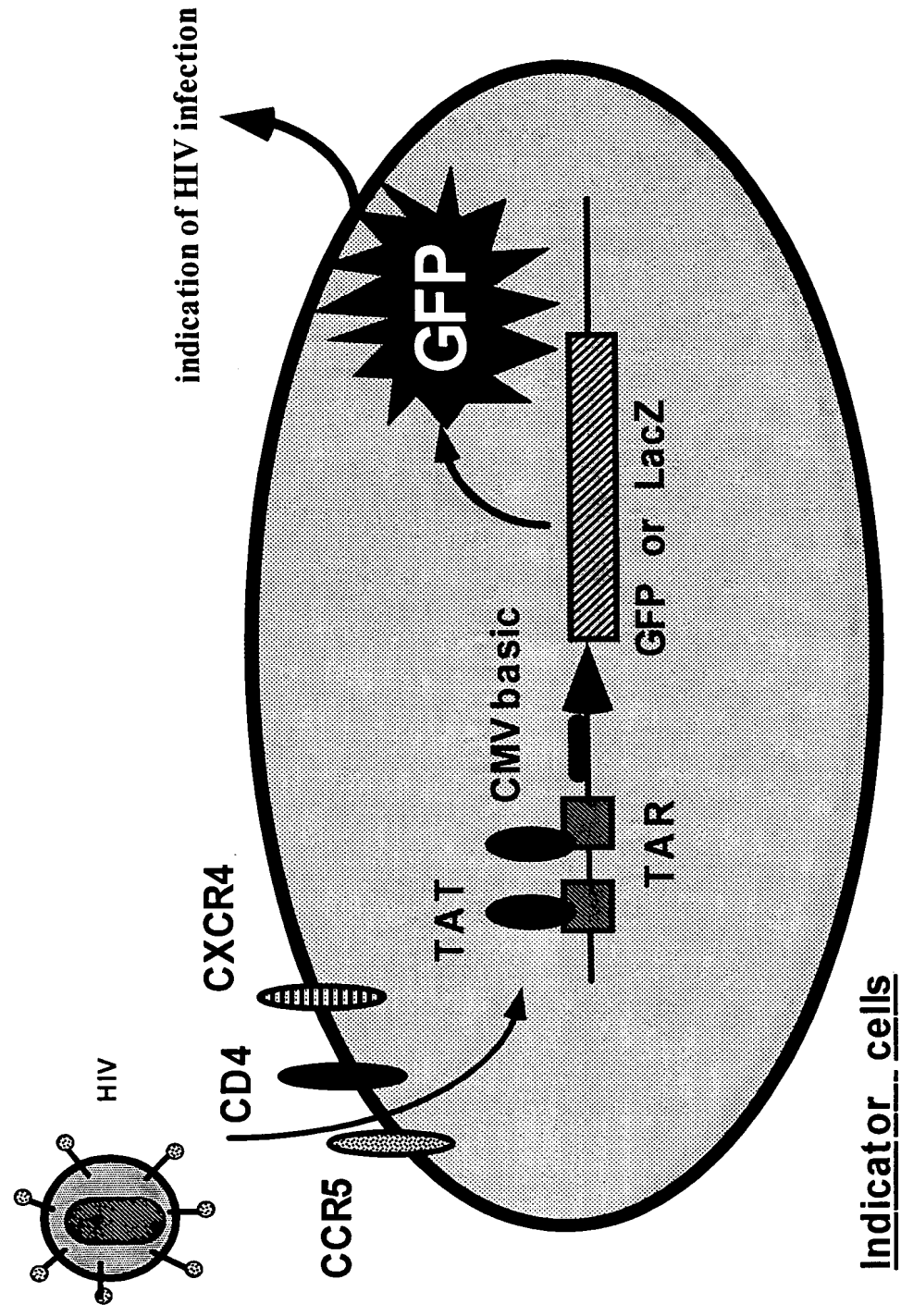


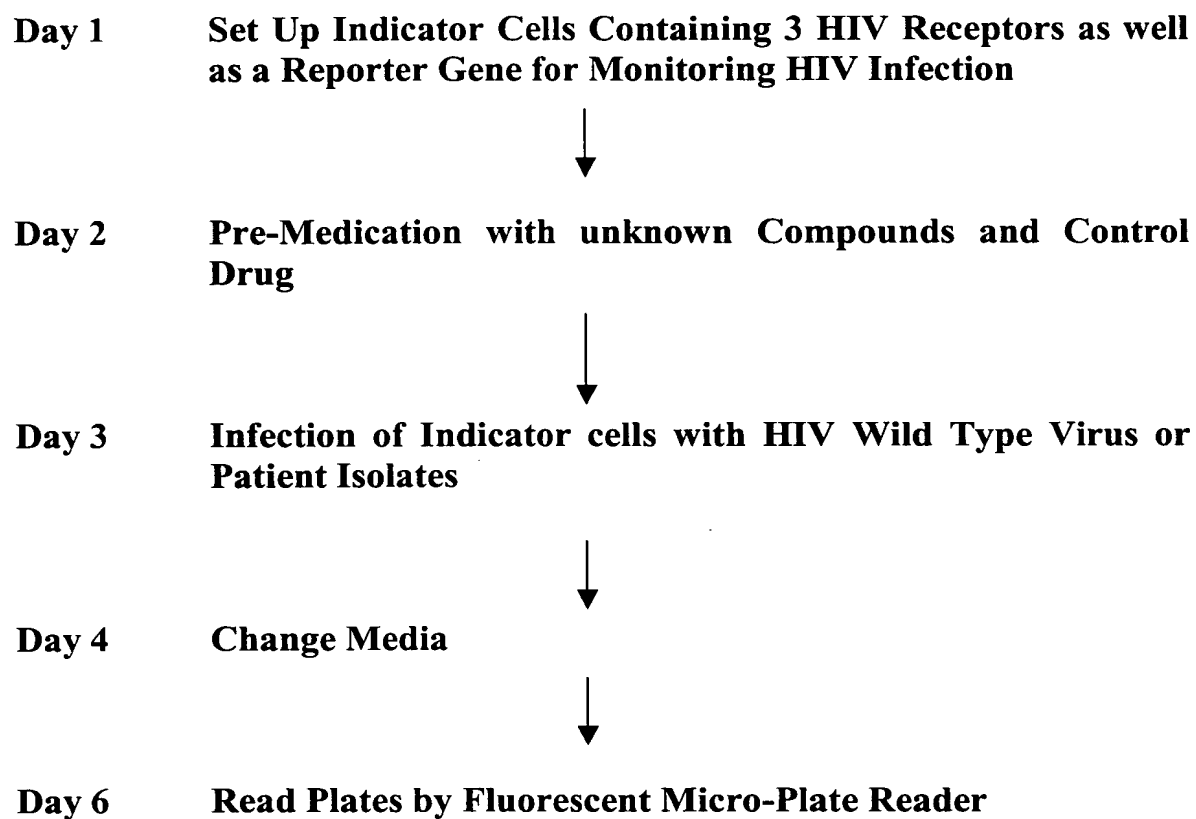
FIGURE 19

Mechanism of the HIV infection indicator cells



**FIGURE 20**

**HIV DRUG SCREENING ASSAY FOR ESI**



## **FIGURE 21**

### **HIV DRUG SCREENING ASSAY FOR LSI**

#### **PRIMARY PLATE**

**Set Up Infection Plate of Cells Containing 3 HIV Receptors  
with HIV in the Presence of a Test Agent  
for a Suitable Period of Time**

#### **SECONDARY PLATE**

**- Day 1      Set Up Indicator Cells Containing 3 HIV Receptors as well  
as a Reporter Gene for Monitoring HIV Infection**



**Day 1      Transfer the Supernatant of the Culture in the Primary  
Plate to the Indicator Cells for Titration of HIV**



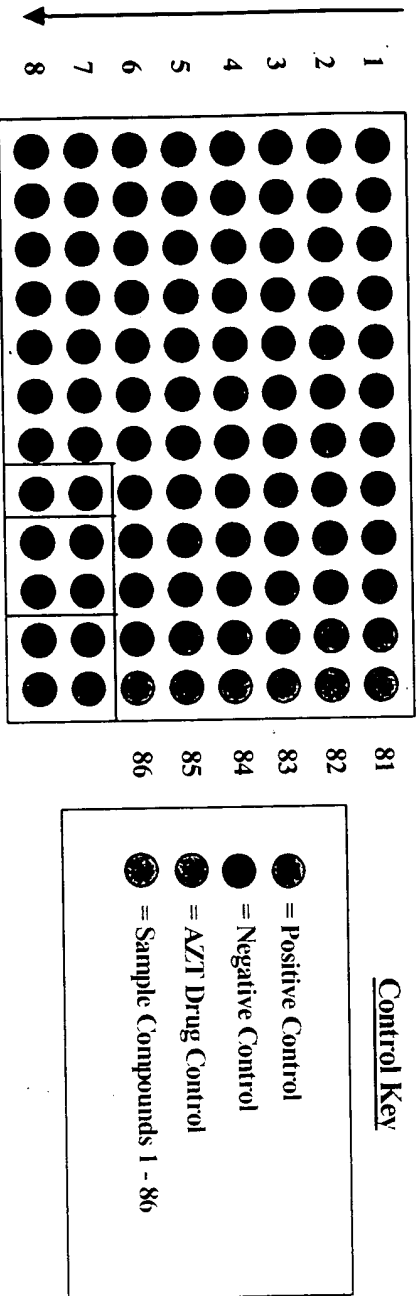
**Day 2      Change Media**



**Day 3-4      Read Plates by Fluorescent Micro-Plate Reader**

FIGURE 22

Phase I Layout



**FIGURE 23**

## Phase II Layout

**(Antiviral assay / Cytotoxicity assay)**

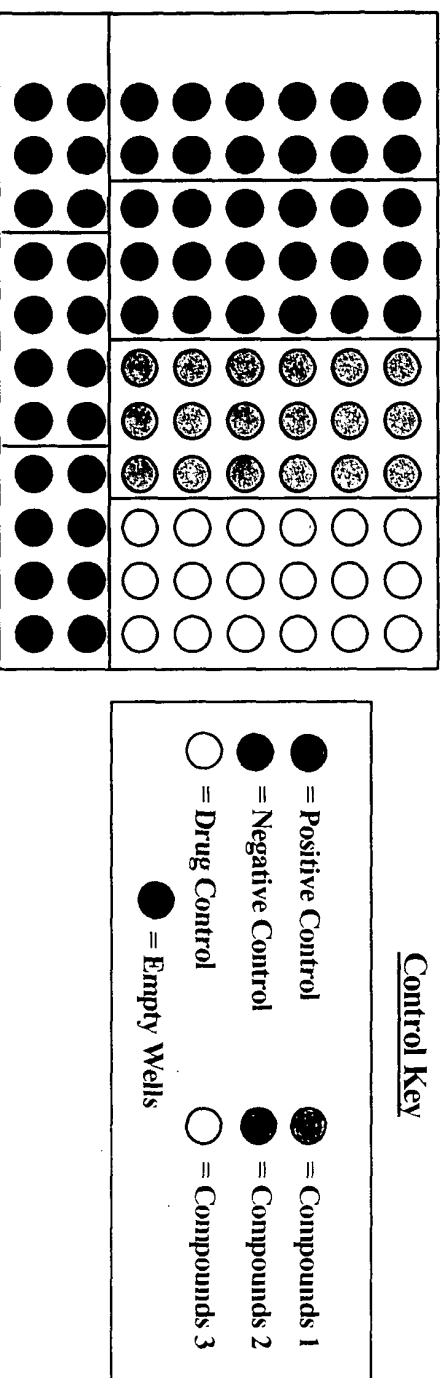




FIGURE 24

Phase III Antiviral Test Layout (WT vs Resistant HIV-1)

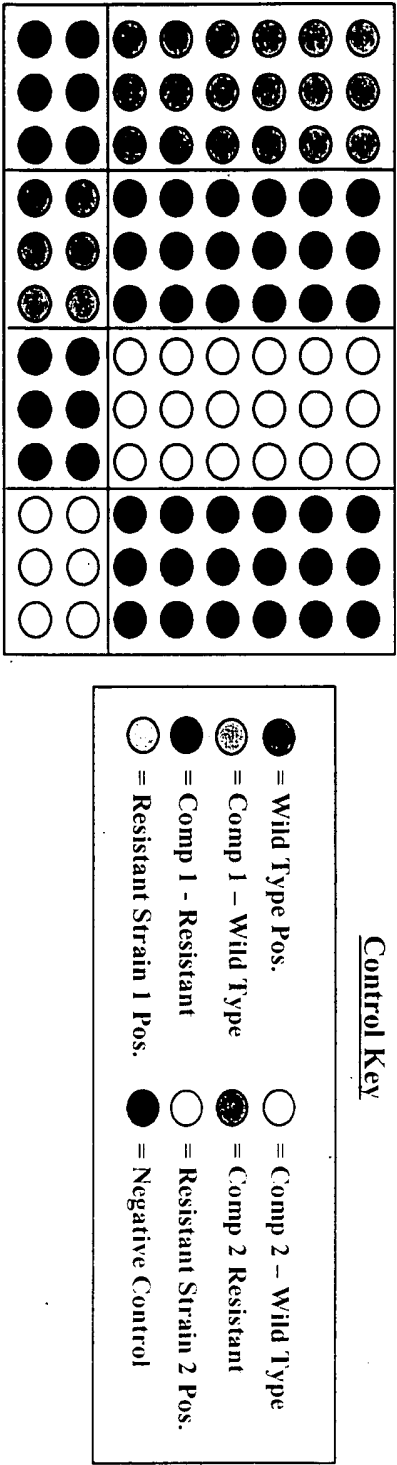


FIGURE 25

Phase I ESI Results

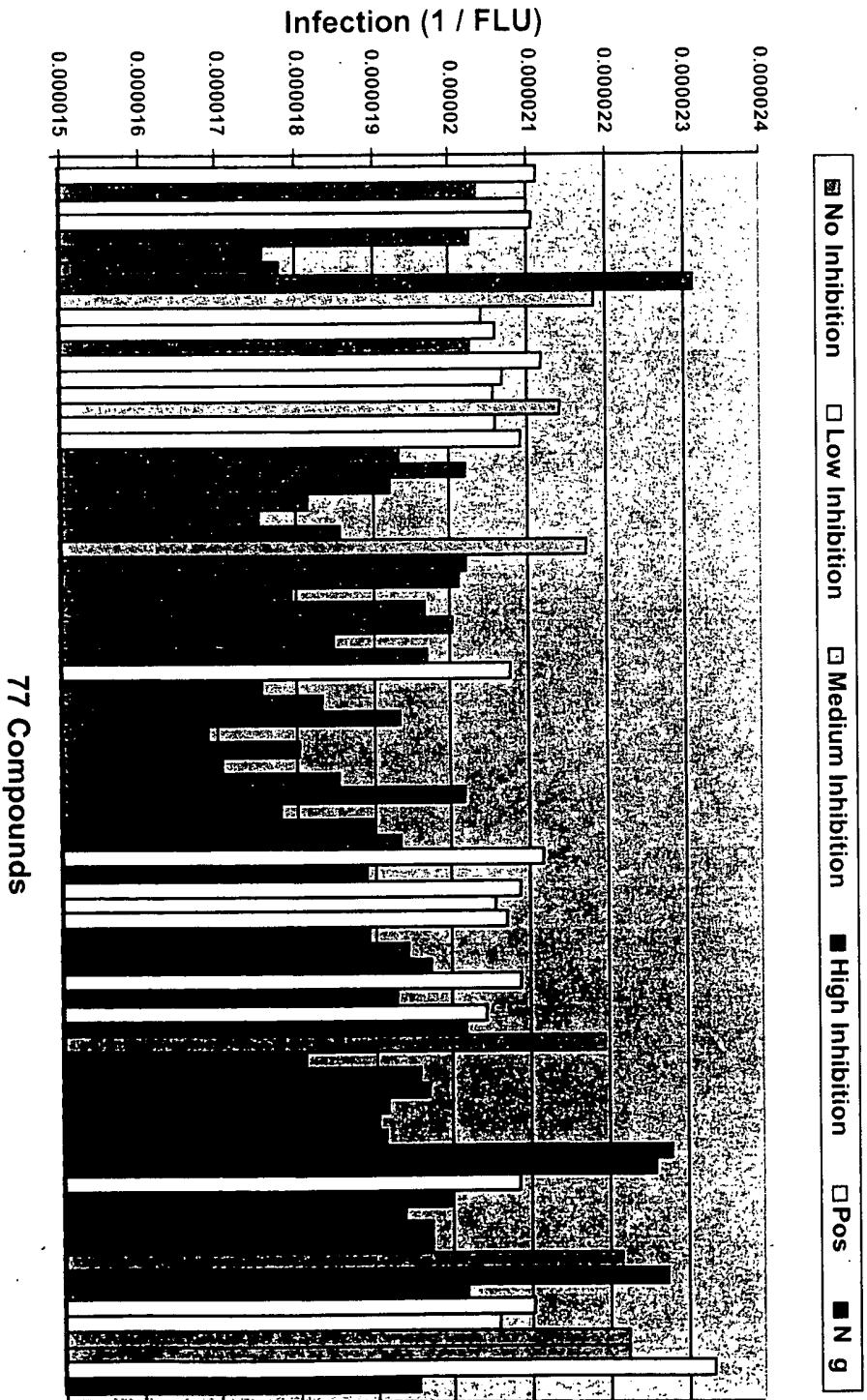


FIGURE 26

Phase I LSI Results

